

**REMARKS**

***Election/Restriction***

Applicants maintain their traversal of the Restriction Requirement mailed on August 17, 2005. Applicants respectfully reserve the right to pursue the non-elected subject matter in one or more continuation, continuation-in-part, and/or divisional applications pursuant to 35 U.S.C. §§ 120 and 121.

***Oath/Declaration***

The Office Action objected to the Oath/Declaration because of informalities.

Applicants are procuring a substitute Oath/Declaration and will submit the substitute Oath/Declaration with the USPTO upon receipt.

***Specification Amendments***

Applicants respectfully request entry of the above amendment to the specification and submit that the above amendments do not constitute new matter. The Amendment submitted herein updates the priority claim in the first line of the specification. Support for the amendment to the specification can be found throughout the specification and in the claims as originally filed.

***Claim Amendments***

Applicants respectfully requests entry of the above amendments to the claims and submit that the above amendments do not constitute new matter. Claims 1-116 have been cancelled. Claims 117, 134, and 148 are amended. Support for the amendments to the claims can be found throughout the specification, *inter alia*, for example, at page 6, lines 19-32; page 8, lines 1-3, 27-33; page 15, lines 24-35; page 18, lines 26-34; and page 19, lines 17-26 of the specification and in the claims as originally filed.

***Claim Objections***

The Office Action objected to claim 6 because of informalities.

Applicants have cancelled claim 6 rendering this objection *moot*.

Reconsideration and withdrawal of the objection is respectfully requested.

***Claim Rejection—35 U.S.C. § 101***

Claims 6-9, 11-24, 117-125, 127-132, 134-137, 140, 141, and 144-148 under 35 U.S.C. § 101 because the claimed invention was allegedly directed to non-statutory subject matter. Applicants respectfully disagree and traverse this rejection.

Claims 6, 26, 40, and 57 have been cancelled rendering the rejection of these claims *moot*.

Claim 117 has been amended per the Office Action suggestion at page 5 rendering this rejection *moot*.

Reconsideration and withdrawal of the rejection is respectfully requested.

***Claim Rejection—35 U.S.C. § 112 ¶ 2***

Claims 17, 117-125, 127-132, 134-137, 140, 141, and 144-148 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants respectfully disagree and traverse this rejection.

Specifically, claim 17 was rejected as vague and indefinite. Claim 17 has been cancelled rendering this rejection *moot*.

Claim 117 was rejected as vague and indefinite. Claim 117 has been amended rendering this rejection *moot*.

Claim 134 was rejected as vague and indefinite. Claim 134 has been amended rendering this rejection *moot*.

Reconsideration and withdrawal of the rejection is respectfully requested.

***Claim Rejection—35 U.S.C. § 102(e)***

Claims 6-8, 16-18, 22, 117-119, 121, 144, and 145 were rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 5,215,899 (“Dattagupta”). Applicants respectfully disagree and traverse this rejection.

Applicants respectfully note that “Dattagupta” was incorrectly cited as “5,215,889” in the Office Action but correctly listed on the PTO-892 form.

Claims 6-8, 16-18, and 22 have been cancelled rendering this rejection *moot*.

The present invention of claim 117 is drawn to a nucleic acid displacer composition comprising an isolated single-stranded oligo-or polynucleotide displacer comprising two or more sequences wherein at least one second sequence comprises one or more modified nucleotides which are different and one or more nucleotides that form a mismatch with the receipt polynucleotide, wherein said displacer changes at least one nucleotide or nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide. Since “[a]nticipation under 35 U.S.C. § 102 requires the disclosure in a single piece of prior art of each and every limitation of a claimed invention.” Electro Med. Sys. S.A. v. Cooper Life Sciences, 32 U.S.P.Q.2d 1017, 1019 (Fed. Cir. 1994), Applicants respectfully submits that Dattagupta fails to meet the limitations of the instant claims.

Dattagupta describes a nucleic acid probe comprising a single stranded self-complementary sequence capable of forming, under hybridizing conditions, a hairpin structure having a functional promoter region, and a single stranded probe sequence extending from the 3' end of said self-complementary sequence. Id. at claim 1; Figures 1-3.

In contrast, the instant claims are drawn to a nucleic acid displacer composition comprising an isolated single-stranded oligo-or polynucleotide displacer wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide. This differs from Dattagupta in that the claimed oligo-or polynucleotide displacer changes at least one nucleotide or nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide. While the Office Action asserts that Dattagupta “changes at least one nucleotide or nucleotide sequence in said receipt polynucleotide (ie., C-T mismatch after hybridizing said displace to said recipient polynucleotide) (see column 12)”, Applicants can not find support for this in Dattagupta. Office Action at 8.

Further, dependent claims 118-119, 121, 144, and 145 are directed to additional features of the invention and their patentability needs to be considered separately from that of claim 117, and in light of such additional claimed features. The Office Action does not establish how or

where each and every limitation of these dependent claims is taught or suggested by the cited references. In re Lee, 277 F.3d 1338, 61 USPQ 2d 1430 (Fed. Cir. 2002)

Reconsideration and withdrawal of the rejection is respectfully requested.

***Claim Rejection— 35 U.S.C. § 102(b)***

Claims 23, 24, and 148 were rejected under 35 U.S.C. § 102(b) as anticipated by Maniatis *et al.* (1978) Cell 15: 687-701. Applicants respectfully disagree and traverse this rejection.

Claims 23-24 have been cancelled rendering this rejection *moot*.

Claim 148 is dependent on claims 118-147, the limitations of which are not taught by Maniatis *et al.*

Reconsideration and withdrawal of the rejection is respectfully requested.

***Claim Rejection— 35 U.S.C. § 103***

Claims 6-9, 16-18, 22, 117-119, 121, 125, 144, and 145 were rejected under 35 U.S.C. § 103(a) as unpatentable over U.S. Patent No. 5,215,899 (“Dattagupta”) and U.S. Patent No. 5,098,890 (“Gewirtz”). Applicants respectfully disagree and traverse this rejection.

A proper obviousness rejection of patent application claims under 35 U.S.C. § 103(a) requires a showing by the USPTO that the invention defined in the rejected claim(s) as a whole is obvious in view of one reference or a combination of the references. M.P.E.P. § 2142. Three basic criteria must be met to support a *prima facie* case of obviousness: (a) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine the reference(s) teachings; (b) there must be a reasonable expectation of success; and (c) the prior art reference (or references when combined) must teach or suggest all the claim features. M.P.E.P. § 2143. Here, the references cited in the Office Action do not individually or in combination suggest to a person of ordinary skill in the art the invention of the Applicants’ claims 117-119, 121, 125, 144, and 145.

Claims 6-9, 16-18, and 22 have been cancelled rendering this rejection *moot*.

The Office Action asserts that Dattagupta discloses a nucleic acid displacer composition. Office Action at 8. The Office Action noted that the differences between the Dattagupta and the claims are that Dattagupta does not disclose:

at least one of the nucleotides complementary to one strand of the recipient polydeoxynucleotide duplex is modified to increase the stability of the hybrid displacer-recipient duplex as recited in claim 9 and at least one of the nucleotides complementary to one strand of the recipient polydeoxynucleotide duplex is modified to increase the stability of the displacer-recipient complex, wherein the modification is in the second sequence as recited in claim 125. Office Action at 11-12.

To fill this gap, the Office Action asserts that Gewirtz discloses that, “substituting a methyl group or sulfur atom for a phosphate oxygen in the internucleotide phosphodiester linkage of A, dA, G, dG, C, dC, T, and U of polynucleotide would make polynucleotides more resistant to nuclease digestion.” Office Action at 12.

The Office Action concluded that one of ordinary skill in the art would have found it obvious to modify Dattagupta using the information from Gewirtz. Id. at 12. The Office Action asserted that one of ordinary skill in the art, “would have been motivated to do so because Gewirtz *et al.*, suggest[ed] that substituting a methyl group or sulfur atom for a phosphate oxygen in the internucleotide phosphodiester linkage of A, dA, G, dG, C, dC, T, and U of polynucleotide would make polynucleotides more resistant to nuclease digestion.” Id. at 12. The Office Action also asserts that one of ordinary skill in the art, “would have [been] [had] a reasonable expectation of success to make [a] the nucleic acid displacer recited in claim 123 in view of the prior art of Dattagupta and Gewirtz *et al.*.” Id. at 12-13.

As discussed above, Dattagupta does not disclose the instantly claimed oligo-or polynucleotide displacer. Id. at Col. 9 line 48 to Col. 11 line 23.

Gewirtz discloses antisense oligonucleotides hybridizable to the *c-myb* mRNA transcript. Id. at Col. 3 line 29 to Col. 4 line 15.

Applicants submit that the references cited in the Office Action do not individually or in combination suggest to a person of ordinary skill in the art the invention of the Applicants’ claim 117 or the remaining claims subject to this rejection.

The Office Action fails to establish why or how it would have been obvious to one of ordinary skill in the art at the time of the invention to combine Dattagupta with Gewirtz to produce an oligo- or polydeoxynucleotide displacer meeting all the limitations of claim 117.

The Office Action does not present a valid motivation or reasonable expectation of success but merely restates the alleged teachings of Gewirtz. MPEP § 2143.01 teaches that a statement that the combination of references to meet the limitations of the claims would have been “well within the ordinary skill of the art at the time the claimed invention was made” because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. Ex parte Levengood, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). See also In re Kotzab, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1318 (Fed. Cir. 2000) (Court reversed obviousness rejection involving technologically simple concept because there was no finding as to the principle or specific understanding within the knowledge of a skilled artisan that would have motivated the skilled artisan to make the claimed invention); Al-Site Corp. v. VSI Int'l Inc., 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999) (The level of skill in the art cannot be relied upon to provide the suggestion to combine references.) Therefore the Office Action does not offer sufficient motivation to combine Dattagupta with Gewirtz. Additionally, the Office Action does not present a valid reasonable expectation of success but merely restates the alleged teachings of Dattagupta and Gewirtz. See MPEP § 2143.02.

Finally, even if, *arguendo*, it were proper to combine the references, it has not been established in the Office Action that the combination would have yielded a method that meets each and every limitation of the claims. The Dattagupta hairpin probe and the currently claimed oligo- or polynucleotide displacer are distinct and, absent an explicit teaching or a suggestion in Dattagupta it would not have been obvious to a person of ordinary skill in the art, to modify the hairpin probe described by Dattapugta. Thus, a person of ordinary skill in the art would not have found it obvious to combine the teachings of Dattagupta and Gewirtz to create an oligo- or polynucleotide displacer at least because neither Dattagupta nor Gewirtz teaches each and every limitation of the claims. Neither Dattagupta nor Gewirtz applied in this rejection suggest the desirability of modifying Dattagupta and any of the improper combinations of the references

would have failed to suggest to a person of ordinary skill in the art the use of the hairpin probe of Dattagupta to produce the oligo- or polynucleotide displacer required by claim 117.

Further, dependent claims 118-119, 121, 125, 144, and 145 are directed to additional features of the invention and their patentability needs to be considered separately from that of claim 117. The Office Action does not delineate how or where each and every limitation of these dependent claims is taught or suggested by the cited references. In re Lee, 277 F.3d 1338, 61 USPQ 2d 1430 (Fed. Cir. 2002).

In accordance with In re Lee, it is improper for the USPTO to make a rejection under 35 U.S.C. § 103(a) by citing references and asserting that it would have been obvious to combine the references in the absence of evidence supporting the assertion that there is a teaching, motivation or suggestion to select and combine the references. To establish a *prima facie* case of obviousness of a claimed invention, the Office Action must establish that each limitation of the rejected independent and dependent claims is taught or suggested by the prior art.

M.P.E.P. § 2143.03. The Office Action failed to do so at least because no evidence was presented that prior art teaches or suggests all limitations of the rejected claims.

Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 6-8, 16-22, 117-119, 121, and 144-147 were rejected under 35 U.S.C. § 103(a) as unpatentable over U.S. Patent No. 5,215,889 (“Dattagupta”) and U.S. Patent No. 5,260,433 (“Engelhardt”). Applicants respectfully disagree and traverse this rejection.

Claims 6-8 and 16-22 have been cancelled rendering this rejection *moot*.

The Office Action asserts that Dattagupta discloses a nucleic acid displacer composition. Office Action at 8. The Office Action noted that the differences between the Dattagupta and the claims are that Dattagupta does not disclose:

that the displacer-linker duplex of claim 6 which contains a modification which allows capture of the displacer-recipient hybrid of affinity chromatography as recited in claim 19 wherein the modification is selected from the group consisting of biotin moieties and phosphorothioate linkages as recited in claim 20 and the modification is present in the linker as recited in claim 21, and said modification in claim 144 is selected from the group consisting of biotin moieties, phosphorothioate linkages and antigens as recited in claim 146 and a modification which allows capture of the displacer-recipient complex by affinity chromatography as recited in claim 147. Office Action at 13.

To fill this gap, the Office Action asserts that Engelhardt discloses polynucleotides which are chemically modified or labeled. Office Action at 13.

The Office Action concluded that one of ordinary skill in the art would have found it obvious to modify Dattagupta using the information from Engelhardt. Id. at 13-14. The Office Action asserted that one of ordinary skill in the art would have been motivated because of the teachings of Engelhardt. Id. at 14. The Office Action also asserts that one of ordinary skill in the art would have had a reasonable expectation of success because of the alleged prior art. Id. at 14-15.

As discussed above, Dattagupta does not describe the instantly claimed oligo-or polynucleotide displacer. Id. at Col. 9 line 48 to Col. 11 line 23; contrast with Figure 1 of the application.

Furthermore, the instant application is assigned to Enzo Biochem, Inc. and Engelhardt is assigned to Enzo Diagnostics, Inc. Enzo Biochem, Inc. and Enzo Diagnostics, Inc. are commonly owned and therefore Engelhardt is not a valid reference pursuant to 35 U.S.C. § 103(c). See Statement of Common Ownership pursuant to M.P.E.P. § 706.02(l)(2). Therefore, it is legally improper to combine Dattagupta with Engelhardt for purposes of an obviousness rejection under 35 U.S.C.

§ 103(a).

Further, dependent claims 118-119, 121, and 144-147 are directed to additional features of the invention and their patentability needs to be considered separately from that of claim 117. The Office Action does not delineate how or where each and every limitation of these dependent claims is taught or suggested by the cited references. In accordance with In re Lee, it is improper for the USPTO to make a rejection under 35 U.S.C. § 103(a) by citing references and asserting that it would have been obvious to combine the references in the absence of evidence supporting the assertion that there is a teaching, motivation or suggestion to select and combine the references. To establish a *prima facie* case of obviousness of a claimed invention, the Office Action must establish that each limitation of the rejected independent and dependent claims is taught or suggested by the prior art. M.P.E.P. § 2143.03. The Office Action failed to do so at

least because no evidence was presented that prior art teaches or suggests all limitations of the rejected claims.

Reconsideration and withdrawal of the rejection is respectfully requested.

***Double Patenting***

Claims 6-9 and 11-24 were rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 6-9 and 11-24 of prior U.S. Patent No. 5,958,681 (“Dattagupta”). Applicants respectfully disagree and traverse this rejection.

Claims 6-9 and 11-24 have been cancelled rendering this rejection *moot*.

Reconsideration and withdrawal of the rejection is respectfully requested.

**CONCLUSION**

Applicants respectfully submits that claims are in condition for allowance, and such disposition is earnestly solicited. Should the Examiner believe that any patentability issues remain after consideration of this Response, the Examiner is invited to contact the Applicants' undersigned representative to discuss and resolve such issues.

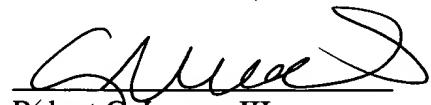
In the event that a variance exists between the amount tendered and that deemed necessary by the U.S. Patent and Trademark Office to enter and consider this Response or to maintain the present application pending, please credit or charge such variance to the undersigned's **Deposit Account No. 50-0206**.

Respectfully submitted,

HUNTON & WILLIAMS LLP

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